American Journal of Medical Genetics 62:91–97 (1996)

Standard Curves of Chest Circumference in Achondroplasia and the Relationship of Chest Circumference to Respiratory Problems

Alasdair G.W. Hunter, Cheryl S. Reid, Richard M. Pauli, and Charles I. Scott, Jr.

Department of Genetics, Children's Hospital of Eastern Ontario, Ottawa, Ontario, Canada (A.G.W.H.); Division of Genetics, Cooper Hospital / University Medical Center, Camden, New Jersey (C.S.R.), Departments of Pediatrics and Medical Genetics, University of Wisconsin, Madison, Wisconsin (R.M.P.), and Division of Genetics, Alfred I. DuPont Institute, Wilmington, Delaware (C.I.S.)

Several pathogenetic factors, alone or in combination, may contribute to the increased frequency of respiratory complications in achondroplasia. It has been suggested that relatively small chest circumference sometimes may contribute. However, there are no published curves of chest circumference for age in achondroplasia with which to compare patients. Nor are there data relating chest circumference to overall size in achondroplasia. We present curves of chest circumference for males and females with achondroplasia from birth through age 7 years. Additional curves for chest circumference against height are also provided. Finally, we report some preliminary data regarding the possible association of chest size with respiratory signs and symptoms.

KEY WORDS: achondroplasia, chest circumference, growth curves, respiratory complications

INTRODUCTION

Respiratory signs and symptoms, such as apnea or pneumonia, are frequently observed in achondroplasia. The prevalence of these complaints varies with the method of patient selection, but was demonstrated to be about 12% (10 of 85) in the clinic population studied by Stokes et al. [1983]. This is in contrast to the 0.92% of American children under age 15 years who are admitted to hospital for pneumonia, acute respiratory infections, or bronchitis/asthma [Bureau of the Census, 1993]. A number of pathogenetic mechanisms may play a role, including diminished chest size with mechanical dysfunction [Hull and Barnes, 1972; Stokes et al., 1983; Reid et al., 1987], upper airway obstruction due to midface hypoplasia and/or upper airway anomalies [Stokes et al., 1983; Reid et al., 1987; Waters et al., 1993], and cervicomedullary compression (CMC) [Yang et al., 1977; Fremion et al., 1984; Waters et al., 1993]. A high rate of apnea and sudden, unexpected death in infants with achondroplasia appear mainly due to the latter factor [Pauli et al., 1984, 1995], which has led to a focus of interest on this aspect of the problem [Nelson et al., 1988; Mador and Tobin, 1990; Waters et al., 1993]. While most authors draw a distinction between central apnea due to CMC and obstructive apnea due to upper airway abnormalities [Reid et al., 1987; Waters et al., 1993], others have hypothesized that CMC may cause obstructive apnea on a central basis [Nelson et al., 1988].

It remains unclear whether reduced chest size in achondroplasia is of clinical significance in the absence of the other proposed mechanisms of respiratory compromise [Stokes et al., 1990], or whether any such effect is directly due to mechanical abnormalities or results from underlying pulmonary hypoplasia. Reduced lung weight has been reported in a stillborn child with achondroplasia [Finegold et al., 1971], and pneumonia remains a significant cause of death in this condition [Hecht et al., 1987]. Conversely, abnormalities of pulmonary function in adolescents and adults with achondroplasia are limited to a reduction of vital capacity [Stokes et al., 1990]. Not all apnea or unexpected death in achondroplasia can be attributed to CMC [Bland and Emery, 1982]; not all patients see significant improvement after decompressive surgery [Reid et al., 1987], while others respond to apparently unrelated treatments such as intracranial shunting and tracheostomy [Mador and Tobin, 1990].

Stokes et al. [1983] posited that hypoxemia, airway closure, and atelectasis in young patients were due to changes in the mechanical properties of the rib cage, and considered that the severity of hypoxemia in individuals with achondroplasia might correlate with reduction in chest size. On the other hand, Nelson et al.

Received for publication June 7, 1995; revision received September 14, 1995.

Address reprint requests to Dr. Alasdair Hunter, Department of Genetics, Children's Hospital of Eastern Ontario, 401 Smyth Rd., Ottawa, Ontario K1H 8L1, Canada.

[1988], while noting that 13 of their 14 patients had a small chest as compared with average stature standards, did not believe there was a correlation between chest size and the severity of respiratory complications.

Against this background there are no standard curves for the chest circumference (cc) in achondroplasia. Stokes et al. [1983] suggested, because thoracic length in achondroplasia was near normal, that general population curves could be used for comparison. However, sitting height data in achondroplasia appear to show a reduced trunk length when compared to the population mean [Horton et al., 1977], and sternal and rib lengths are reduced in achondroplasia. Also, whether the growth rate of the chest is similar in average statured individuals and those with achondroplasia is unknown. Here we present standard curves of chest circumference for age and height in achondroplasia, and compare the measurements of patients reported to have had respiratory problems against those standards.

PATIENTS AND METHODS

Patient Population

The number and origin of individuals and number of chest measurements are shown in Table I. Most measurements were obtained at times of initial assessment and routine follow-up visits, and most often were recorded by the same examiner over time. Others were obtained through solicitation for volunteers as part of an ongoing study (by A.G.W.H.) or at conventions of Little People of America, Inc. (LPA) (by C.S.R.).

Data and Analysis

Chest measurements were taken in the standard fashion at the nipple line, using a nonstretching tape [Hall et al., 1989]. In the case of mature females, measurement was taken by having the patient lift the breasts and running the tape underneath. Medical histories were obtained from clinic records and through direct patient/parent interview. All respiratory symptoms were scored regardless of whether they could reasonably be attributed to a lung problem. Note was also made of whether the patient had been documented as having obstructive sleep apnea and/or a foramen magnum decompression.

Data were entered into Statistical Package for Social Scientists (SPSS/PC+) for calculation of means and standard deviations by age and by height. The data were scanned visually and by trend of standard deviation (SD) for data entry errors. The patients were grouped by month to age 2 years, by 3 months from 2 to age 6 years, and by 6 months thereafter. Heights were grouped in 2-cm intervals; heights were from Delaware, Australia, or the United Kingdom. The number of measurements in each age and height category are shown in Table II. The results were transferred to Harvard graphics to produce unsmoothed curves of means, ±1 SD and ±2 SD.

TABLE I. Source and Number of Subjects and of Chest Measurements

Source	Number of subjects	Number of measurements
Delaware	92	433
Wisconsin	40	177
New Jersey (LPA)	167	226
Australia	53	87
United Kingdom	13	13
Total	365	936

RESULTS AND DISCUSSION

The raw data curves were very similar for males and females. The curves were very smooth from ages 2–10 years. Slightly greater unevenness below age 24 months may reflect proportionately greater measurement errors in young infants, but was mostly a result of graphing by monthly intervals. This produces fewer measurements per point. Inadequate data made the curves unreliable beyond age 10 years, and obesity, rather than actual growth of the chest, probably accounted for a rise in circumference beyond age 20 years. Manually smoothed curves were produced for ages 0–24 months and for birth to age 7 years because these are the years of maximum interest, and because these are ages for which data points were adequate in number.

Figure 1 presents the smoothed curves of the data for males, and Figure 2 for females, from birth to age 7 years. The mean, ±1 and ±2 SD, are shown (solid lines), together with the mean and −2 SD curves for the general population (dotted lines). The average-statured population data are from the Boston Collaborative Study, which included a similar number of measure-

TABLE II. Mean and Range of Number of Data Points of Chest Circumference Recorded at Each Age and Height

	Age categories					
	0–24 months, 1-month interval		27–72 months, 3-month interval		6.5–9 years, 6-month interval	
	Mean	Range	Mean	Range	Mean	Range
Male	7.5	4–15	12.8	6–19	7.9	5–13
Female	6.6	2–13	10.4	3–15	6.0	4–10

	Height (length) from 46–108 cm	
	Mean	Range
Male	7.9	2–20
Female	5.8	1–14

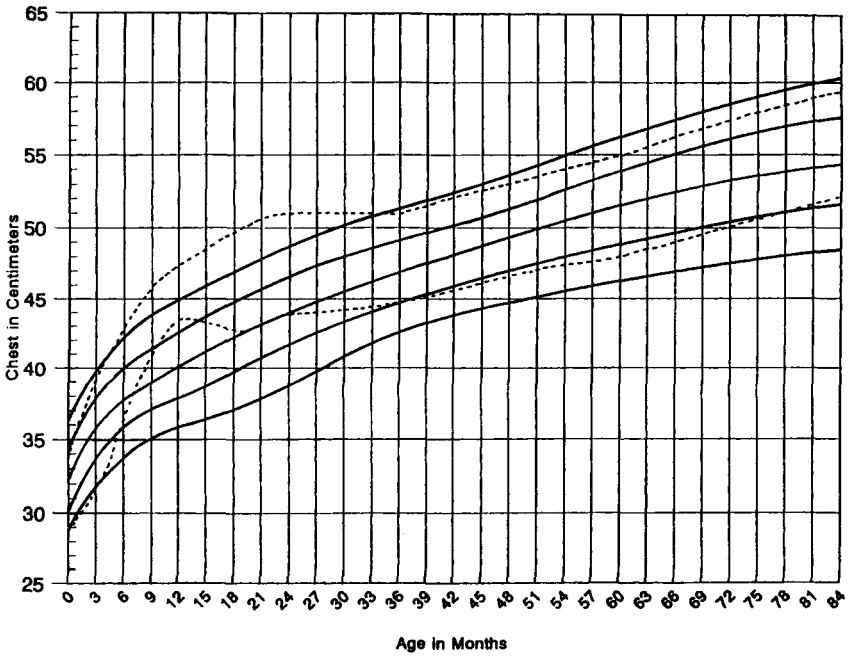

Fig. 1. Smoothed curves (solid lines) of male mean chest circumference, ±1 and ±2 SD from birth to age 7 years. The general population mean is shown above, and −2 SD below (dotted lines), for comparison.

ments and were published as smoothed curves of combined male and female measurements [Feingold and Bossert, 1974]. However, the actual comparisons were made with graphs provided by Marilyn Preus (McGill University, Montreal, Canada) because they had been subject to less dramatic smoothing, and because they also allowed distinction between male and female. However, given that both the normative and achondroplasia data sets have been smoothed, comparisons should be made with caution. Variation in SD over age, of both the general and achondroplastic population, is partly an artifact due to limited sampling and partly the reflection of a natural increase in variance with age. At term birth, the mean chest circumference in achondroplasia is about 2–2.5 cm less than in the general population, and the general population mean lies at +1

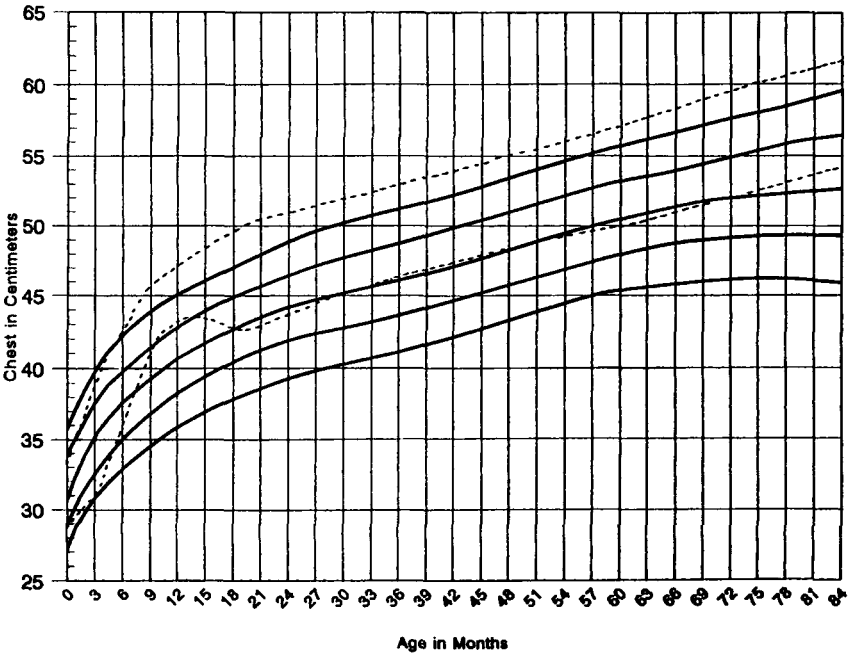

Fig. 2. Smoothed curves (solid lines) of female mean chest circumference, ±1 and ±2 SD from birth to age 7 years. The general population mean is shown above, and −2 SD below (dotted lines), for comparison.

SD for achondroplasia. From about 2–15 months the rate of growth of the chest in achondroplasia appears to lag behind that of the general population; it then shows some catch-up to about age 3 years, after which time the curves are fairly parallel. In the average-stature population the chest circumference in females is about 2 cm larger than in males from ages 2–12 years. In contrast, chest circumference in males with achondroplasia overtakes that of females at about age 3 years. From age 18 months the mean chest circumference of females with achondroplasia approximates the 3rd centile of the general population, while in males it is the −1 SD that parallels the general-population −2 SD curve from about 3 years.

Figure 3a,b provides respective smoothed curves of the mean and ±1 and ±2 SD, from birth to age 24 months for males and females with achondroplasia. These graphs should be suitable for the routine assessment and follow-up of young children with achondroplasia.

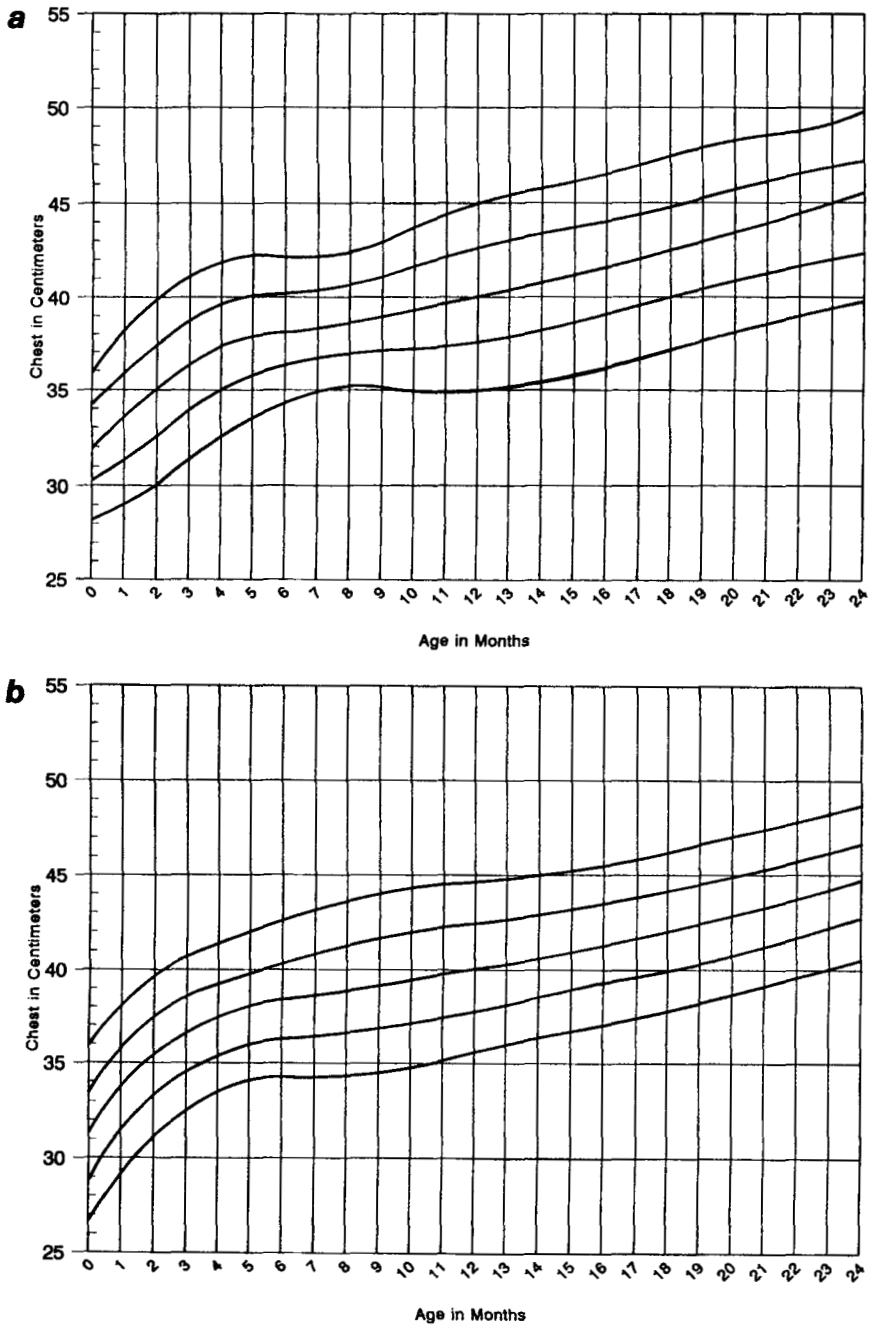

Fig. 3. Respective male (**a**) and female (**b**) smoothed curves of mean chest circumference, ±1 and ±2 SD from birth to age 24 months.

We considered that the rate of growth in chest circumference might parallel the general rate of skeletal growth, and thus show a more linear relationship with height than with age. Indeed, in this population sample the correlation coefficient for chest circumference with age is 0.83, as compared to 0.96 with height and 0.95 with weight. The high correlation with weight may at first seem puzzling, until one considers that height and weight are themselves highly correlated with one another (0.93, Hunter et al., submitted], and that chest circumference will, to some extent, reflect central obesity, in much the same way as subscapular skin fold. Four hundred and ninety-seven concurrent height and chest circumference measurements were available. Figure 4a,b shows the mean and ±1 and ±2 SD of chest circumference for height, for males and females, respectively. In both instances the curves are relatively straight, with narrow standard deviations. Up to 58 cm (typical height for age 6 months), females appear to have a slightly larger chest circumference for a given length, but from 58–108 cm (approximately age 10 years), the means show no significant difference. Suitable data beyond 108 cm were not available. These curves may be useful in assessing whether a given patient has a disproportionately small chest.

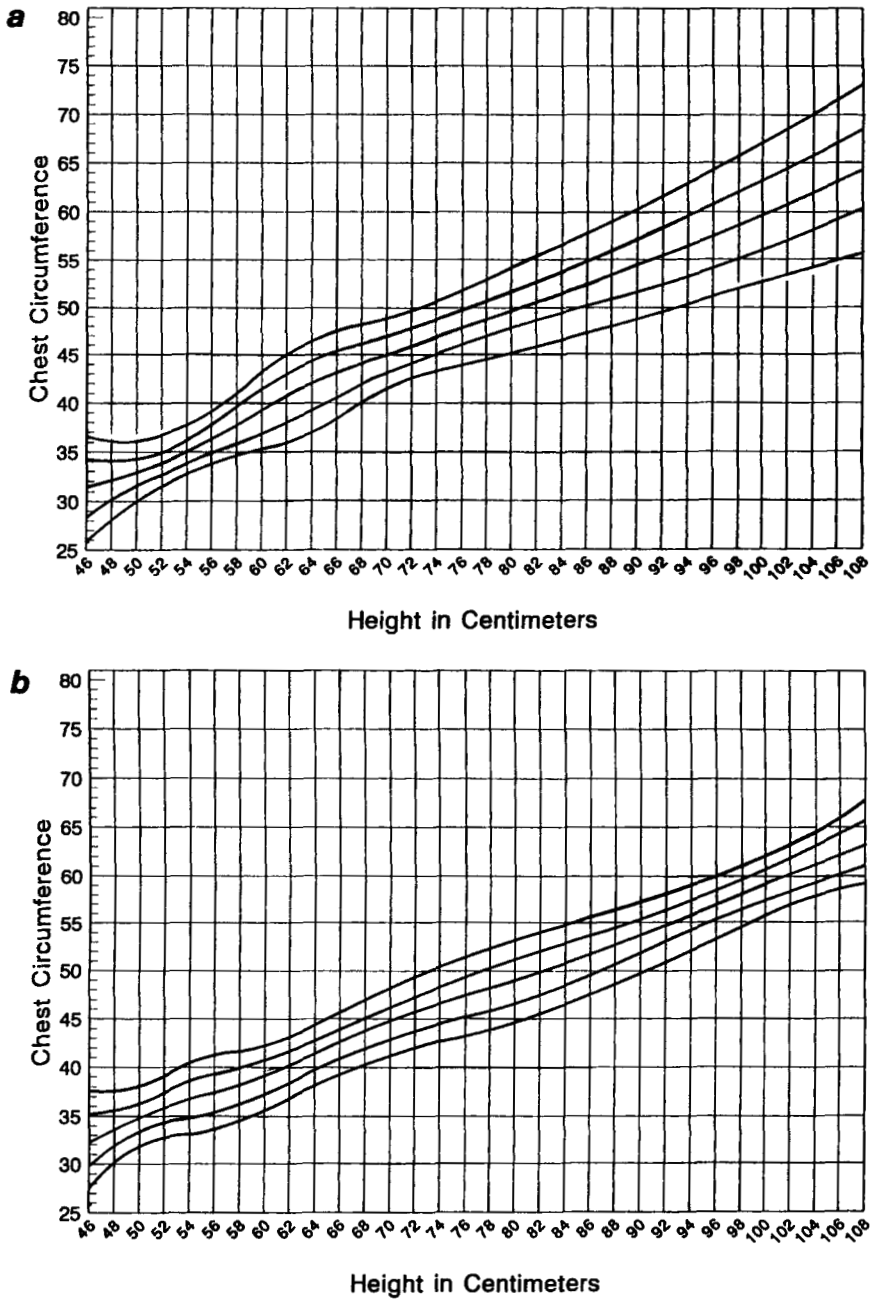

Fig. 4. Male (**a**) and female (**b**) chest circumferences plotted against height, giving mean ±1 and ±2 SD.

TABLE III. Distribution of Standard Deviation of Chest Circumference for Age in Patients With Respiratory Problems

Major respiratory complication	Total no. of patients	Standard deviation of chest circumference			
		>+1 SD–<2 SD	±1 SD	<−1 SD–>−2 SD	<2 SD
Cor pulmonale	10	1	5	2	2
Pneumonia	26	0	18	6	2
Apnea[a]	23	3	16	3	1
Supplementary oxygen[b]	15	1	9	4	1
Obstructive sleep apnea	16	3	9	3	1
Total	90	8	57	18	7

[a]Four had foramen magnum decompression.
[b]Several documented hypoxemic during sleep.

Table III shows the distribution of the standard deviations from the age- and sex-appropriate mean of chest measurements of patients known to have had respiratory signs. The history of an individual patient was often complex, and it was generally not possible to determine unequivocally the primary cause of a specific respiratory complication. Therefore, what appeared to be the clinically most important problem was used to categorize each patient, who was then tabulated under only one diagnosis. Where more than one chest measurement was available on the same patient, the youngest age was used to plot the subject on the appropriate smoothed curve of chest circumference. Measurements in those with respiratory abnormalities often did not coincide temporally with the illness. Notwithstanding the limitations of this retrospective analysis, it is of note that 28% (25/90) of patients had a CC of less than −1 SD, whereas 16% (14.4/90) would be expected (chi-square test, $P < 0.01$). This downward shift in CC is most apparent for cor pulmonale and pneumonia. There were 47 males and 43 females among the 90 patients. There were too few concurrent chest and height measurements for patients who also had respiratory dysfunction to allow an assessment of whether respiratory problems are associated with a disproportionately small chest for a given height.

CONCLUSIONS

The impression that some respiratory problems seen in achondroplasia occur secondarily to reduced chest circumference remains an unproven hypothesis. As an initial step in assessing this question we have provided standard curves of chest circumference for age and for height that will allow for prospective evaluation of subjects with achondroplasia. Average chest circumferences at all ages are reduced when compared with average-statured individuals. Early growth of chest circumference seems to be particularly impaired.

ACKNOWLEDGMENTS

A.G.W.H. thanks David Danks, David Sillence, Dian Donnai, and Helen Hughes, who welcomed him into their departments and allowed access to their patients and records. He thanks Dr. John Rogers, Dr. Agnes Bankier, Dr. Kay Metcalfe, Dr. Jonathan Gray, Mrs. Barbara Bedwell, Ms. Anne Cronin, Mrs. Jo Wells, Ms. Karmel Burtuccio, Ms. Margo Latham, Ms. Julie Rotta, and Ms. Mary Carten who, in various permutations and combinations, helped by pulling charts, contacting patients, arranging accommodations, sharing their offices, and providing secretarial help, clinical advice, and friendship. This study would have been impossible without the support and encouragement of Little People of America, Inc., and the willingness of the individuals and families affected by chondrodysplasias to open their homes to our visits. The support of the Children's Hospital of Eastern Ontario for a sabbatical year is gratefully acknowledged. A final and special thank you to my wife Hedda who skillfully drove through unfamiliar cities to home visits and waited patiently. We also acknowledge V. Kim Horton, R.N., M.S., Catherine A. Reiser, M.S., Lisa P. Glinski, M.S., and Christina Palmer, Ph.D., for their contributions to the collection of data in Madison, Wisconsin.

REFERENCES

Bland JD, Emery JL (1982): Unexpected death of children with achondroplasia after the perinatal period. Dev Med Child Neurol 24: 489–492.

Bureau of the Census (1993): "Statistical Abstract of the United States: 1993," 113th ed. Washington, DC: p 126.

Feingold M, Bossert WH (1974): Normal values for selected physical parameters: An aid to syndrome delineation. White Plains, New York: The National Foundation—March of Dimes. BD:OAS X (13):1–16.

Finegold MJ, Katsew H, Genieser NB, Becker MH (1971): Lung structure in thoracic dystrophy. Am J Dis Child 122:153–159.

Fremion AS, Bhuwan PG, Kalsbeck J (1984): Apnea as the sole manifestation of cord compression in achondroplasia. J Pediatr 104:398–401.

Hall JG, Froster-Iskenius UG, Allanson JE (1989): "Handbook of Normal Physical Measurements." Oxford: Oxford University Press, pp 293–295.

Hecht JT, Francomano CA, Horton WA, Annegers JF (1987): Mortality in achondroplasia. Am J Hum Genet 41:454–464.

Horton WA, Rotter JI, Kaitila I, Gursky J, Hall JG, Shepard TH, Rimoin DL (1977): Growth curves in achondroplasia. New York: Alan R. Liss, Inc. The National Foundation—March of Dimes. BD:OAS XIII (3C):101–107.

Hull D, Barnes ND (1972): Children with small chests. Arch Dis Child 47:12–19.

Mador MJ, Tobin MJ (1990): Apnestic breathing. A characteristic feature of brainstem compression in achondroplasia? Chest 97:877–883.

Nelson FW, Hecht JT, Horton WA, Butler IJ, Goldie WD, Miner M (1988): Neurological basis of respiratory complications in achondroplasia. Ann Neurol 24:89–93.

Pauli RM, Scott CI, Wassman ER, Gilbert EN, Leavitt LA, Ver Hoeve J, Hall JG, Partington MW, Jones KL, Sommer A, Feldman W,

Langer LO, Rimoin DL, Hecht JT, Lebovitz R (1984): Apnea and sudden unexpected death in infants with achondroplasia. J Pediatr 104:342–348.

Pauli RM, Horton VK, Glinski LP, Reiser CA (1995): Prospective assessment of risks for cervico-medullary junction compression in infants with achondroplasia. Am J Hum Genet 56:732–744.

Reid CS, Pyeritz RE, Kopits SE, Maria BL, Wang H, McPherson RW, Hurko O, Philips JA III, Rosenbaum AE (1987): Cervicomedullary compression in young patients with achondroplasia: Value of comprehensive neurologic and respiratory evaluation. J Pediatr 110: 522–530.

Stokes DC, Phillips JA, Leonard CO, Dorst JP, Kopits SE, Tojak JE, Brown DL (1983): Respiratory complications in achondroplasia. J Pediatr 102:534–541.

Stokes DC, Wohn ME, Wise RA, Pyeritz RE, Fairclough DL (1990): The lungs and airways in achondroplasia: Do little people have little lungs? Chest 98:145–152.

Waters KA, Everett F, Sillence D, Fagan E, Sullivan CE (1993): Breathing abnormalities in sleep in achondroplasia. Arch Dis Child 69:191–196.

Yang SS, Cortett DP, Brough AJ, Heidelberger KP, Bernstein J (1977): Upper cervical myelopathy in achondroplasia. Am J Clin Pathol 68:68–72.